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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,591	01/04/2002	Bruce D. Cohen	ABX-PF2 US	1445

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,591	COHEN ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,23-27 and 29-150* is/are pending in the application.

4a) Of the above claim(s) *20,23-27,29-33 and 122-150* is/are withdrawn from consideration.

5)☒ Claim(s) *36-52,56,59-72,74-93,95,98-117 and 119* is/are allowed.

6)☒ Claim(s) *34,53,55,57,58,73,94,96,97,118 and 120* is/are rejected.

7)☒ Claim(s) *35 and 121* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/01/04, 10/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-19, 21-22, 28 have been canceled.

Claims 34-150 have been added.

2. Claims 20, 23-27, 29-33 and newly added claims 122-150 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. Applicant timely traversed the restriction (election) requirement in Paper filed 4/15/04.

3. Claims 34-121 are under examination.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains some NEW GROUNDS of rejection.

Rejections Withdrawn

6. The rejection of claims 3-6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

8. The rejection of claims 5-6, 15-17 under 35 U.S.C. ' 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is

withdrawn in view of the declaration stating that all assurances have been met for deposit.

7. The rejection of claims 3-4 and 17 are rejected under 35 U.S.C. 112, first paragraph is withdrawn in view of the amendments to the claims.

8. The rejection of claims 1-6 under 35 U.S.C. 102(e) as being anticipated by Fujita-Yamaguchi (US 2003/0165502, priority to 6/00) is withdrawn in view of the amendments to the claims.

9. The rejection of claims 1-6 under 35 U.S.C. 103(a) as being unpatentable over Kucherlapati et al (US Patent 6,657,103, filed 9/97) and further in view of Rubini et al (Experimental cell research 251:22-32, 1999) is withdrawn in view of the amendments to the claims.

10. The rejection of claims 1-6 under 35 U.S.C. 103(a) as being unpatentable over Rubini et al (Experimental cell research 251:22-32, 1999) and further in view of Adair et al (WO 91/09967, published 7/91) is withdrawn in view of the amendments to the claims.

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 112

11. Claims 34, 53, 55, 57-58, 73, 94, 96-97, 118, 120 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an

isolated antibody that binds IGF-IR and has the CDR sequences of the variable domain of the light chain of 2.13.2 or SEQ ID NO:6 or the variable domain of the heavy chain of 2.13.2 or SEQ OD NO:8 or from the variable domain of SEQ ID NO:6 and 8 or the antibody has a heavy chain variable domain that utilizes the human DP-47 gene or a light chain variable domain that utilizes a human A30 gene, does not reasonably provide enablement for any antibody that has one or two CDRS from a light/or heavy chain and one or two CDRs from a heavy/or light chain or an antibody that utilizes the DP-47 gene with at least one amino acid substitution in SEQ ID NO:45 or an antibody that utilizes the A30 gene with at least one substitution in SEQ ID NO:47. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to antibodies which have CDRs mixed from heavy and light chains. For example CDR1 from a light chain and CDR2 and/or 3 from a heavy chain. Claims 53 and 55 are broadly drawn to antibodies with at least one substitution in SEQ ID NO:45 or 47. The specification teaches the CDR sequences of

the 2.12.1 and 2.13.2, but does not enable antibodies as broadly claimed. The scope of the claims is not commensurate with the scope of enablement provided in the specification.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. In addition, Colman (Research in immunology 145:33-36, 1994) teach that example of antigen-antibody interactions paint a confusing picture and a conservative substitution may abolish binding (see page 35). Thus, it is unlikely that antibodies as defined by the claims

which may contain CDRs of the light chain and the heavy chain in the same variable domain or contain only one substitution in SEQ ID NO:45 or 47 as compared to the DP-47 or A30 gene, have the required binding function. As indicated above the CDRs have to be in the correct frameworks for binding and claims 53 and 55 only require at least one substitution as in SEQ ID NO: 45 or 47 and as such the claims are broadly drawn to antibodies that have the DP-47 gene with only one substitution and as such it would not bind because the antibody requires the entire variable region of SEQ ID NO:45 or 47 for complete binding. The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

12. Claim 54 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 54 recites the limitation of "utilizes the human VH3-23 gene". Support for the limitation is stated to be to be on page 19-30 of the specification (see page 22 of

response). In response to this argument, the examiner failed to find the term "VH3-23 anywhere in the cited pages. Applicant is required to provide specific support for the claim limitation in the specification as originally filed or remove it from the claim.

Conclusion

13. Claims 36-52, 56, 59-72, 74-93, 95, 98-117, 119 are in condition for allowance. Claim 35 and 121 are objected to as depending from a rejected claim.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is ~~703-872-9306:~~ 571 273 8300

Respectfully,

Larry R. Helms Ph.D.

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER